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Lifetime Vigorous But Not Light-To-Moderate Habitual Physical Activity Impacts Favorably on Carotid Stiffness in Young Adults

The Amsterdam Growth and Health Longitudinal Study

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Abstract—Higher levels of habitual physical activity favorably impact on arterial stiffness. It is not clear, however, whether lifetime habitual physical activities of different intensities carry the same protective effect and to what extent any such effect is mediated by other biological cardiovascular risk factors. We, therefore, examined longitudinal data on habitual physical activity and cardiovascular risk factors (8 repeated measures between the ages of 13 and 36 years) in 373 subjects in whom stiffness estimates of the carotid artery were assessed at age 36 years using noninvasive ultrasonography. The time spent in habitual physical activities (in minutes per week) throughout the longitudinal period was compared between subjects across tertiles of the following stiffness estimates: β-stiffness index, distensibility and compliance coefficients, and the Young's elastic modulus. After adjustments for sex, body height, and other lifestyle variables, subjects in the highest tertile of the β-stiffness index (ie, with stiffer arteries) had spent, on average, throughout the longitudinal period, less time in vigorous (−26.5 [95% CI: −45.9 to −7.1]) but less so in light-to-moderate habitual physical activities (−11.2 [95% CI: −53.5 to 31.1]) as compared with subjects in the lowest tertile. The difference in time spent in vigorous activities was greatly attenuated when further adjusted for blood lipids, cardiorespiratory fitness, fat distribution, resting heart rate, and mean arterial pressure (to −11.2 [95% CI: −29.4 to 7.0]). Similar results were found for the other stiffness estimates. Promoting vigorous intensity physical activities among the healthy young may, therefore, prevent arterial stiffness and related cardiovascular sequelae later in life, partly through its favorable impact on other biological cardiovascular risk factors. **(*Hypertension*. 2010;55:33-39.)**

Key Words: exercise ■ arteriosclerosis ■ adolescence ■ young adults ■ risk factors ■ life course ■ epidemiology

Higher levels of habitual physical activity (HPA) attenuate the increase in arterial stiffness that occurs with ageing.[1] Given that stiffening of central (ie, elastic) arteries, such as the aorta and carotid arteries, increases the risk of cardiovascular disease,[2] maintaining a physically active lifestyle in the course of life may, thus, constitute a valuable tool to reduce arterial stiffness-related cardiovascular disease.[3]

The evidence so far underlining the beneficial role of HPA on aortic or carotid stiffness has been derived from both cross-sectional observational studies showing that subjects who are more physically active have less stiff arteries than their sedentary counterparts[4–7] and intervention studies showing favorable arterial adaptations after increases in aerobic exercise.[6,8,9] However, the fact that aerobic exercise has been ineffective in the restoration of arterial distensibility in some clinical populations, for example, in elderly individuals with isolated systolic hypertension,[10] suggests that increases in HPA are likely more effective when initiated early in life.

Arterial stiffness has its roots early in life. From this perspective, we[11] and others[12,13] have shown previously that higher levels of body fatness and blood pressure in childhood/adolescence are associated with increased arterial stiffness in adulthood. Higher levels of HPA protect against the development of such biological cardiovascular risk factors among the young,[14] and these effects may, thus, provide a mechanism through which HPA prevents the development of arterial stiffness later in life. However, it is not clear to what extent HPAs of different intensities carry the same protective effect on both arterial stiffness and other cardiovascular risk factors among the young. For instance, some studies have

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shown that vigorous but not light-intensity HPAs were associated with less arterial stiffness.[4,15,16] From a preventive point of view, addressing these complex interrelationships is of utmost importance to construct targeted interventions with the highest potential for health benefits.

In view of these considerations, we have, therefore, investigated, in a cohort of healthy young individuals whose HPA levels and cardiovascular risk factors have repeatedly been assessed from ages 13 to 36 and in whom stiffness estimates of the carotid artery could be assessed at age 36: first, whether the mean levels and the developmental patterns, from adolescence up to adulthood, of light-to-moderate and vigorous HPAs differed between subjects with stiffer versus those with less stiff carotid arteries in adulthood; and second, the extent to which any such differences were explained by a favorable impact of HPAs (if any) on other cardiovascular risk factors.

Methods

Subjects and Study Design

All of the subjects were participants of the Amsterdam Growth and Health Longitudinal Study. This study started in 1977 with a group of ≈600 boys and girls from 2 secondary schools in The Netherlands. Its initial goal was to describe the natural development of growth, health, and lifestyle of adolescents and to investigate longitudinal relations between biological and lifestyle variables, as described in detail elsewhere.[17] The mean age of the subjects at the beginning of the study was 13.1 (±0.8) years. Since then, measurements were obtained 2 to 8 times (ie, at the ages of 13, 14, 15, 16, 21, 27, 32, and 36) during a 24-year follow-up period. At each measurement, anthropometric, biological, and lifestyle variables were assessed. In 2000, when the subjects' mean age was 36.5 (±0.6) years, arterial properties were assessed for the first time in 377 subjects.[11,18,19] The present study reports on 373 subjects (196 women) in whom complete arterial data were available.

The study was approved by the medical ethical committee of the VU University Medical Center (Amsterdam, The Netherlands). All of the subjects gave their written informed consent (provided by their parents when subjects were 13 to 16 years old).

Arterial Stiffness

When subjects were 36 years old, arterial properties of the carotid, brachial, and femoral arteries were assessed by means of noninvasive ultrasonography according to guidelines for user procedures and with the use of reproducible and valid methods and devices.[2,20,21] All of the subjects had abstained from smoking and caffeine-containing beverages on the day that the measurements were performed. Measurements took place after subjects had been resting in a supine position for 15 minutes in a quiet, temperature-controlled room. Properties of the right common carotid artery (10 mm proximal to the beginning of the bulb) were obtained by 2 trained vascular sonographers with the use of an ultrasound scanner equipped with a 7.5-MHz linear array probe (Pie Medical). The ultrasound scanner was connected to a personal computer equipped with an acquisition system and a vessel wall movement detector software system (Wall Track System 2, Pie Medical). This integrated device enabled measurements of arterial diameter (D), distension (ΔD), and intima-media thickness (IMT), as described in detail elsewhere.[20,21]

Throughout the entire period of ultrasound imaging, systolic (SP), diastolic (DP), and mean arterial blood pressure were assessed in the left arm at 5-minute intervals with an oscillometric device (Colin Press-Mate, model BP-8800). Brachial pulse pressure (PP) was defined as SP−DP, and PP at the level of the common carotid artery was calculated by calibration of the distension waveforms.[22] The mean carotid IMT, D, ΔD, SP, DP, and local PP of 3 consecutive measurements (each including 3 to 7 heartbeats) were used to estimate the β-stiffness index (SI), the distensibility coefficient (DC), the compliance coefficient (CC), and the Young's elastic modulus (E_{inc}), as follows[11,12,18,19]:

$$SI = \ln(SP/DP)/(\Delta D/D) \quad (1)$$

$$DC = (2\Delta D \cdot D + \Delta D^2)/(PP \cdot D^2) \text{ in } 10^{-3}/\text{kPa} \quad (2)$$

$$CC = \pi \cdot (2D \cdot \Delta D + \Delta D^2)/4PP \text{ in } \text{mm}^2/\text{kPa} \quad (3)$$

$$E_{inc} = D/(IMT \cdot DC) \text{ in } 10^3 \cdot \text{kPa} \quad (4)$$

Habitual Physical Activity

HPA was measured at each measurement occasion (ie, from age 13 to 36 years) by means of a structured, detailed face-to-face interview. At the mean ages of 27 and 32 years, a standard form containing cues was used during the HPA interview,[23] and, at the mean age of 36, an identical interviewer-administered, computer-assisted version was introduced. The interview covered the preceding 3 months, except when subjects were of the opinion that their HPA pattern during this period was abnormal (eg, because of illness or holiday), and was always performed during the same time of the year (ie, between January and June). The intensity, frequency, and duration of all of the physical activities (at school, at work, at home, during leisure time, in organized and unorganized sports, climbing stairs, and in active transportation) with a duration of ≥5 minutes and exceeding an intensity level of 4 times the resting metabolic rate (ie, >4 metabolic equivalents; METs) were retrieved. According to their intensities, activities were then classified into light-to-moderate (4 to 7 METs, eg, brisk walking), hard (7 to 10 METs, eg, tennis or jogging), and very hard (>10 METs, eg, squash). Extreme values of HPA at given time points, that is, those >3 SD from the time-specific mean level, were excluded from the analyses, and time spent in hard and very hard-intensity HPAs were combined into a "vigorous" intensity category.

Covariates

Throughout the 24-year study period, other lifestyle (ie, alcohol consumption, smoking behavior, and dietary intake), anthropometric (ie, body height, body weight, and body skinfolds), and biological (ie, sitting blood pressure, cardiorespiratory fitness, blood lipids, and resting heart rate) risk factors were measured as described in detail elsewhere.[11,17–19,23,24]

Statistical Analyses

We used generalized estimating equations to investigate the mean difference in time spent in light-to-moderate and vigorous HPAs, throughout the 24-year longitudinal period (ie, from age 13 to 36 years), between subjects in the higher sex-specific tertiles (ie, T2 or T3) versus those in the lowest tertile (T1) of the carotid SI, DC, CC, and E_{inc} at age 36 years. Before categorization into tertiles, the DC and CC were inversed so that higher values indicate higher stiffness levels in accordance with the SI and the E_{inc}. The longitudinal method of data analyses adopted adjusts for the correlation between repeated observations taken in the same subject and has the advantage of handling repeated data of subjects with varying numbers and unequally time-spaced observations.[25] The analyses were first adjusted for sex, body height (to account for subject growth throughout the longitudinal period), and time (entered in the model as a continuous variable; model 1) and subsequently for other lifestyle risk factors, that is, smoking and alcohol drinking status (yes or no) and total energy intake (in kilocalories per day), all considered as potential confounders (model 2). Next, we further adjusted for other biological cardiovascular risk factors, that is, mean arterial pressure, skinfold ratio (as a marker of central pattern of fat distribution),[11] cardiorespiratory fitness, total:high density lipoprotein (HDL) cholesterol ratio, and resting heart rate, to ascertain the extent to which any differences in HPAs between the groups being compared could be explained (ie, mediated) by the favorable impact of HPA on these risk factors (models 3a to 3e and 4). Thus, these analyses enabled us to ascertain the presence of any such "mediating effect" by examining the magnitude of the changes in differences in HPA levels

Table 1. Characteristics of the Study Population Throughout the 24-Year Longitudinal Period

	Calendar Age, y							
Variables	13	14	15	16	21	27	32	36
HPA								
Total, min/wk	579±192	548±197	548±226	516±198	513±299	452±313	499±303	745±455
Light-to-moderate, min/wk	281±142	310±159	375±196	366±182	427±269	354±305	369±268	628±449
Vigorous, min/wk	298±160	237±125	172±103	150±97	85±114	98±94	130±138	117±99
Other lifestyle risk factors								
Alcohol consumption, %	13.5	15.9	33.3	48.2	69.0	72.5	80.3	82.1
Smoking, %	1.6	11.0	14.0	17.9	29.9	26.2	20.2	23.5
Total energy intake, 1000 kcal/d	2.46±0.55	2.51±0.59	2.59±0.68	2.55±0.68	2.62±0.73	2.48±0.64	2.60±0.71	2.62±0.70
Biological risk factors								
Systolic blood pressure, mm Hg*	124.7±9.3	123.3±9.2	125.2±9.9	126.0±10.6	128.8±11.2	129.5±11.9	129.6±12.4	131.2±14.4
Diastolic blood pressure, mm Hg*	75.5±7.8	75.9±7.6	72.5±8.0	74.6±8.1	78.7±8.4	81.1±8.6	84.6±8.8	85.4±10.6
Mean arterial pressure, mm Hg*	91.9±6.9	91.7±6.6	90.1±6.6	91.8±7.2	95.4±8.0	97.2±8.4	99.6±9.0	100.7±11.0
Pulse pressure, mm Hg*	49.2±9.8	47.4±10.2	52.7±11.9	51.4±11.4	50.1±10.5	48.4±10.7	45.0±9.9	45.8±9.8
Body mass index, kg/m^2	17.7±1.8	18.4±2.0	19.2±2.1	19.8±2.1	21.4±2.2	22.2±2.3	23.3±2.9	24.1±3.1
Sum of 4 skinfolds, mm†	32.0±12.0	33.5±14.0	35.3±15.0	38.9±16.6	44.8±17.2	41.9±16.1	47.4±19.2	51.5±18.2
Skinfold ratio‡	0.49±0.06	0.51±0.06	0.53±0.06	0.55±0.06	0.58±0.08	0.56±0.08	0.56±0.09	0.57±0.10
VO_2 max, mL/min per kg^{FFM}	69.5±6.5	68.9±6.3	67.0±5.7	66.2±6.5	59.8±6.2	56.6±6.4	56.5±7.4	60.6±8.4
Total:HDL cholesterol ratio	3.2±0.7	3.2±0.7	3.4±0.8	3.2±0.7	3.8±0.9	3.8±1.0	3.7±1.2	3.8±1.3
Resting heart rate, bpm	83±14	79±13	79±15	76±14	72±13	72±13	75±14	71±11

Data are mean±SD or percentages. FFM indicates fat-free mass; VO_2 max, maximal oxygen uptake as a marker of cardiorespiratory fitness.
*Measurements were performed with a sphygmomanometer on the right arm with subjects in the sitting position after ≥5 minutes of rest.
†Data show the sum of the thickness of the following skinfolds: triceps, biceps, subscapular, and suprailiac.
‡Ratio calculated as (subscapular+suprailiac)/sum of 4 skinfolds.

between the groups being compared before and after adjustments for these risk factors (in which case these differences would decrease). In these analyses we adjusted for the skinfold ratio instead of the sum of skinfolds or body mass index because of its stronger association with HPAs and carotid stiffness.[11]

Generalized estimating equations were also used to examine the longitudinal associations between time spent in HPAs on the one hand and biological cardiovascular risk factors on the other. Results of these analyses are expressed as standardized longitudinal regression coefficients to enable comparison of the strength of the associations between HPA and each risk factor. These analyses were adjusted for covariates as mentioned above (models 1 and 2).

Finally, we examined the trajectories of the different intensity HPAs, from age 13 to age 36 years, between the groups being compared, by adding interaction terms between group and time to the models described above. Results hereby obtained were displayed graphically (smoothed line plots).[24,25]

In all of the generalized estimating equation analyses, an exchangeable correlation structure was used, which was deemed the most appropriate after examination of the interperiod correlation matrixes of HPA and cardiovascular risk factors throughout the 24-year study period.[25] All of the results are reported for men and women combined, because no significant interactions with sex were found. All of the statistical analyses were performed with the use of the Stata software package version 9.2 (Stata Corp).

Results

Table 1 shows the general characteristics of the study population throughout the longitudinal period. After adjustment for sex and body height, the total time spent in HPA decreased from age 13 to age 27 years (−77 min/wk [95% CI: −143 to −11 min/wk]) followed by a considerable increase thereafter up to the age of 36 years (278 min/wk [95% CI: 225 to 332 min/wk]). The time spent in light-to-moderate HPAs increased by 348 min/wk (95% CI: 295 to 401 min/wk), whereas time spent in vigorous HPAs decreased by 148 min/wk (95% CI: −169 to −126 min/wk) between adolescence and the age of 36 years. The mean values (±SD) of SI, DC, CC, and E_{inc} across tertiles of each stiffness estimate are presented in Table 2.

Lifetime Light-to-Moderate and Vigorous HPAs and Arterial Stiffness in Young Adulthood

Compared with subjects in T1, that is, with a less stiff carotid artery, those in T2 and T3 of the SI, that is, with increasingly higher levels of carotid stiffness at age 36 years, spent on average significantly less time in vigorous HPAs (−25.3 min/wk [95% CI: −45.0 to −5.5 min/wk] and −31.9 min/wk [95% CI: −51.6 to −12.1 min/wk], respectively), throughout

Table 2. Stiffness Levels at the Age of 36 Years Across Tertiles of Each Carotid Stiffness Estimate

Carotid Stiffness Estimates	T1 (Less Stiff)	T2 (Intermediate)	T3 (Stiffer)
SI	6.0±0.5	7.2±0.4	9.0±1.1
DC, 10^{-3}/kPa	33.4±4.1	26.2±1.6	20.3±2.2
CC, mm^2/kPa	1.28±0.20	0.97±0.09	0.72±0.12
E_{inc}, $10^3 \cdot$ kPa	0.32±0.05	0.43±0.03	0.58±0.09

Data are mean±SD. T1 indicates lowest tertile; T2, middle tertile; and T3, highest tertile of each carotid stiffness estimate. All of the stiffness estimates differ significantly across increasing tertiles (*P* for trend: <0.001).

Table 3. Difference in Time Spent in HPAs Throughout the 24-Year Longitudinal Period

		SI			
		T2 vs T1		T3 vs T1	
Model	Adjustments	β	95% CI	β	95% CI
Light-to-moderate HPAs					
1	Sex, height, and time	−10.1	−52.3 to 32.1	−23.2	−65.3 to 19.0
2	Model 1+other lifestyles	−0.3	−42.6 to 41.9	−11.2	−53.5 to 31.1
Vigorous HPAs					
1	Sex, height, and time	−25.3	−45.0 to −5.5*	−31.9	−51.6 to −12.1†
2	Model 1+other lifestyles	−19.5	−38.9 to −0.2*	−26.5	−45.9 to −7.1†
3a	Model 2+mean arterial pressure	−19.0	−38.4 to 0.3	−25.3	−44.8 to −5.9*
3b	Model 2+skinfold ratio	−17.5	−36.5 to 1.4	−21.1	−40.1 to −2.0*
3c	Model 2+cardiorespiratory fitness	−14.5	−33.0 to 4.0	−20.5	−39.1 to −1.9*
3d	Model 2+total:HDL cholesterol ratio	−13.0	−32.6 to 6.6	−20.1	−39.8 to −0.5*
3e	Model 2+resting heart rate	−19.3	−38.2 to −0.4*	−23.9	−42.8 to −4.9*
4	Model 2+all variables in models 3a to 3e	−9.8	−27.8 to 8.2	−11.2	−29.4 to 7.0

β indicates regression coefficient, that is, the average difference in time spent in HPAs (in min/wk) throughout the 24-year longitudinal period between subjects in the middle (T2) and highest (T3) tertiles vs those in the lowest (T1) tertile of the SI.

*$P<0.05$.

†$P<0.01$.

the longitudinal period (Table 3, model 1). In contrast, no significant differences in time spent in light-to-moderate HPAs were found between the groups. Similar associations were found for the other stiffness estimates (Figure 1).

Adjustment for other lifestyle risk factors, that is, potential confounders, attenuated the differences mentioned above in vigorous HPAs between T2 and T3 versus T1 to −19.5 min/wk (95% CI: −38.9 to −0.2 min/wk) and to −26.5 min/wk (95% CI: −45.9 to −7.1 min/wk), respectively (Table 3, model 2). The difference in time spent in vigorous HPAs between subjects with the "stiffer" arteries (ie, T3) versus those with the "less stiff" arteries (ie, T1) at age 36 years was further attenuated when adjusted for the total:HDL cholesterol ratio (by 24%; model 3d), cardiorespiratory fitness (by 23%; model 3c), skinfold ratio (by 20%; model 3b), and resting heart rate (by 10%; model 3e), but not by mean arterial pressure (model 3a). When adjustments accounted for all of these potential mediating risk factors simultaneously, the difference in time spent in vigorous HPAs between subjects in T3 versus those in T1 was attenuated (ie, explained) by ≈58% and was no longer significant (model 4).

Similar results as described above were found when the differences in vigorous HPAs between subjects in T3 versus those in T1 of the carotid DC, CC, or E_{inc} were adjusted for these potential confounders and mediators; only the attenuation after adjustment for mean arterial pressure was relatively greater than the one observed for the SI (although never exceeding 14%) because of the greater dependence of those

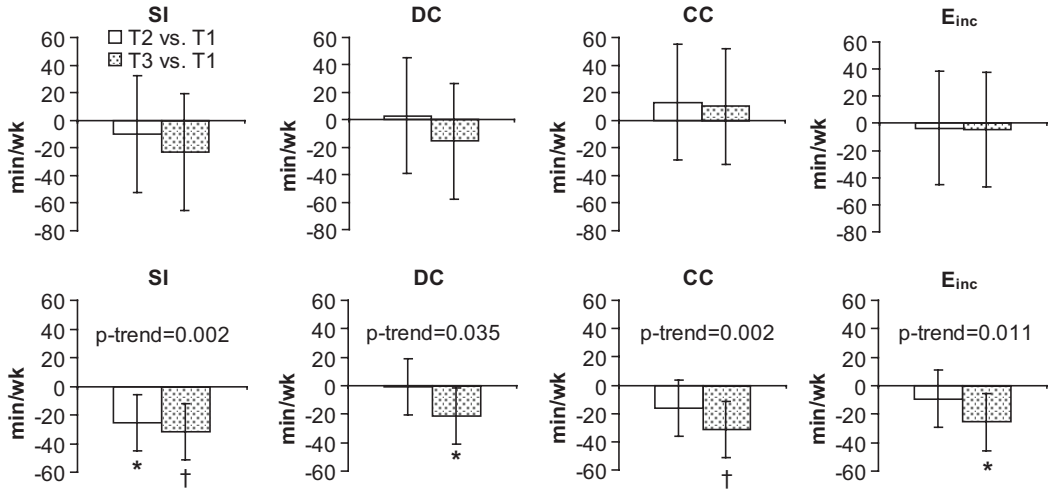

Figure 1. Average differences in time spent in light-to-moderate–intensity (top) and vigorous-intensity (bottom) HPAs throughout the 24-year longitudinal period between subjects in the middle (T2) and highest (T3) tertiles vs those in the lowest tertile (T1) of each carotid stiffness estimate (indicated by bars). Data are adjusted for sex, height, and time; vertical lines indicate the 95% CI around the average differences. *$P<0.05$, †$P<0.01$.

Table 4. Longitudinal Associations Between Time Spent in HPAs and Other Cardiovascular Risk Factors

	Mean Arterial Pressure		Skinfolds Ratio		Cardiorespiratory Fitness ($VO_{2\ max}$)		Total:HDL Cholesterol Ratio		Resting Heart Rate	
Model	β	95% CI	β	95% CI	β	95% CI	β	95% CI	β	95% CI
Time spent in light-to-moderate HPA										
1	−0.023	−0.064 to 0.017	−0.012	−0.044 to 0.021	0.051	0.009 to 0.093*	−0.054	−0.089 to −0.020†	−0.056	−0.096 to −0.017†
2	−0.016	−0.057 to 0.025	−0.011	−0.043 to 0.022	0.035	−0.007 to 0.077	−0.038	−0.072 to −0.003*	−0.047	−0.087 to −0.006*
Time spent in vigorous HPA										
1	−0.072	−0.113 to −0.032†	−0.080	−0.113 to −0.048‡	0.184	0.142 to 0.225‡	−0.111	−0.145 to −0.076‡	−0.135	−0.175 to −0.095‡
2	−0.070	−0.112 to −0.029†	−0.084	−0.117 to −0.051‡	0.171	0.130 to 0.214‡	−0.098	−0.133 to −0.063‡	−0.134	−0.175 to −0.093‡

β indicates standardized longitudinal regression coefficient, that is, the magnitude of the change in biological risk factors (in SD) per 1 SD increase in time spent in HPA. Model 1: adjusted for sex, height, and time; model 2: model 1+adjustments for alcohol consumption, smoking behavior, and total energy intake.

*$P<0.05$.

†$P<0.01$.

‡$P<0.001$.

other estimates on mean arterial pressure than the SI (please see Table S1 in the online Data Supplement, available at http://hyper.ahajournals.org). Indeed, more time spent in HPAs, particularly of vigorous intensity, was favorably associated with all cardiovascular risk factors examined (Table 4, model 1), and adjustments for other lifestyle risk factors attenuated these associations only slightly (model 2).

Life-Course Trajectories of Light-to-Moderate and Vigorous-Intensity HPAs in Subjects With Stiffer Versus Less Stiff Arteries at the Age of 36 Years

All of the groups increased their time spent in light-to-moderate HPAs between adolescence and the age of 36 years, and no marked differences in the patterns of development across groups were observed regarding this type of HPA. Only at the age of 32 years and thereafter did subjects in T1, that is, those with less stiff arteries, tend to spent more time in this type of HPA as compared with those in T2 and T3 of the SI (Figure 2A). In contrast, time spent in vigorous HPAs decreased substantially between adolescence and young adulthood in all of the groups. However, subjects in T2 and T3, that is, those with increasingly higher levels of carotid stiffness, spent less time in these activities than those with less stiff arteries (T1), particularly in late adolescence and thereafter, that is, after the age of ≥15 years to the age of 36 years (Figure 2B).

Essentially, similar patterns of HPAs throughout the course of life were found when subjects were categorized on the basis of levels of DC, CC, and E_{inc} (data not shown).

Discussion

The main findings of this study were 3-fold. First, subjects with stiffer carotid arteries at the age of 36 years (as assessed by different local stiffness estimates) spent significantly less time in vigorous but not in light-to-moderate–intensity HPAs between adolescence and young adulthood, supporting the view of a favorable impact of vigorous HPAs on carotid arterial stiffness. Second, this favorable impact was explained, to a great extent, by the beneficial vigorous HPA-related changes in other cardiovascular disease risk factors. Third, despite considerable decreases in time spent in vigorous HPAs during adolescence in the whole study population, compared with subjects with less stiff arteries, those with stiffer carotid arteries were characterized by steeper decreases in time spent in vigorous HPAs during late adolescence and consistently less times in these HPAs thereafter, up to the age of 36 years.

The beneficial effects of HPA on aortic or carotid stiffness have been widely reported in cross-sectional and intervention studies.[4–9,15,16] We have now examined in detail to what extent the beneficial effects of HPA can be attributed to a relatively higher contribution of time spent in HPAs of different intensities throughout the course of life and identified vigorous-intensity HPAs as the type of HPA carrying the greatest beneficial impact on carotid arterial stiffness. These findings are in line with others showing that activities of higher intensity were associated with less arterial stiffness.[4,15,16] By adopting a life-course approach, we found that, with ageing, subjects spent increasingly more time in light-to-moderate and less time in vigorous HPAs. This shift toward less time spent in vigorous activities started already in adolescence. However, maintenance of relatively higher levels of vigorous-intensity activities from adolescence up to adulthood was associated with lower levels of arterial stiffness several years later, at the age of 36. Therefore, our findings emphasize that the promotion of vigorous-intensity HPA in adolescence and young adulthood, to counteract its critical decline during this period,[26] may be a valuable tool to effectively prevent arterial stiffness-related cardiovascular sequelae later in life.

Current physical activity recommendations in both children[26] and adults[27] do recognize the added value of increasing vigorous HPA for reducing cardiovascular disease but do not explicitly focus on these, because health benefits are thought to result from increases in either light-to-moderate or vigorous HPAs. Although our findings do not dismiss the value of increasing light-to-moderate HPAs, for instance, among those children and young adults who are extremely sedentary and

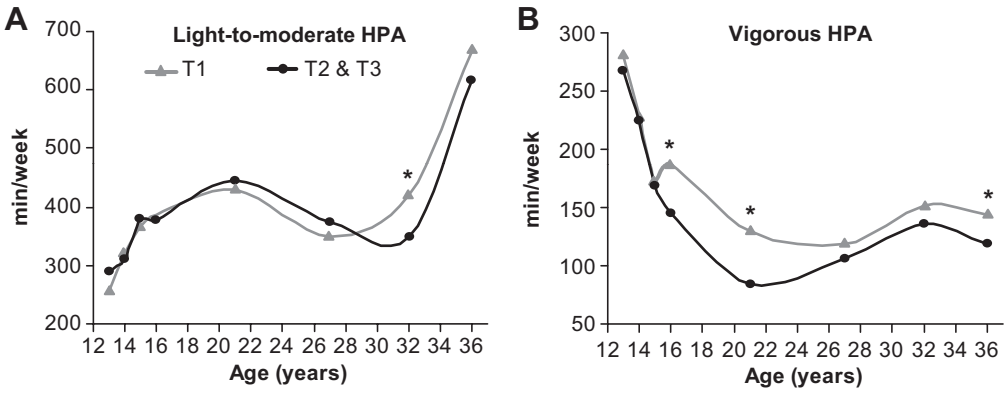

Figure 2. Time spent in (A) light-to-moderate and (B) vigorous HPAs throughout the longitudinal period by subjects in the lowest tertile (T1) and those in the middle and highest tertiles (T2 and T3) of the carotid SI at the age of 36 years. Note that the latter 2 groups were combined because their mean levels of HPAs throughout the longitudinal period were comparable and differed in similar magnitudes from subjects in tertile 1. Data are adjusted for sex, height, and time. *$P<0.05$ (tertiles 2 and 3 vs tertile 1).

usually obese, they emphasize the importance of promoting vigorous HPAs, in particular when targeting the common general young population. This is also supported by the observation that higher levels of vigorous, but less so of light-to-moderate, HPA carried a greater beneficial impact on other biological cardiovascular risk factors. In fact, these vigorous HPA-related improvements in the biological cardiovascular risk factors, which are all known determinants of arterial stiffness,[2,11–13] explained much of the favorable impact of HPA on stiffness levels of the carotid artery. All together, improvements in these cardiovascular risk factors that are intertwined, at least in part, lead to decreased arterial stiffness through mechanisms such as increases in parasympathetic activity,[28] improvement of endothelial function because of enhanced arterial shear stress,[29] reduction of low-grade inflammation,[30] and improvements in insulin sensitivity.[31]

We categorized subjects into tertiles according to the values obtained for each of the carotid stiffness estimates that were assessed at the age of 36 years. This approach allowed us to compare the development of HPA levels from adolescence up to adulthood for subjects with stiffer and those with less stiff carotid arteries in adulthood. The differences in, for instance, the carotid DC and CC values between those in the highest versus those in the lowest tertiles corresponded with values observed in the course of >1 decade of ageing,[32] which illustrates that the groups being compared translate to physiologically relevant differences in mean levels of arterial stiffness.

There are some limitations to our study. First, our findings were confined to subjects attending the follow-up in 2000 in whom complete data on arterial properties could be assessed. However, levels of HPA, as well as blood pressure, body fatness, cardiorespiratory fitness, and blood lipids, in these subjects did not differ, at any earlier time point, from those subjects who dropped out (data not shown), indicating that selection bias is unlikely to have threatened the validity of our findings. Second, carotid stiffness levels were measured at age 36 years only. Therefore, we cannot rule out the possibility that reversed causation may have occurred, that is, that subjects with stiffer arteries at any earlier time point may have been less prone to perform (vigorous) HPAs.[33] Third, in our analyses we did not differentiate between strength and endurance training that could have affected arterial stiffness differently.[1] Indeed, strength exercise has an adverse effect, whereas endurance training has a favorable effect on arterial stiffness. However, the relative contribution of activities carrying a strong component of strength exercise (eg, bodybuilding, weightlifting, wall climbing, rowing, and lifting/carrying heavy objects) amounted <2% of the total time spent in HPAs, contributed similarly to the time spent in light-to-moderate and vigorous HPAs, and was equally distributed across the groups being compared and, thus, did not affect our results. Finally, the assessment of HPA levels by means of questionnaires is subject to recall and misclassification bias.[34] Most likely these biases were nondifferential, because subjects were unaware of their arterial stiffness levels when they reported their HPAs throughout the study period. Still, some differential biases may have occurred, probably by overreporting of HPA levels by those with unhealthier lifestyles/risk-factor profiles. Either way, the differences in HPA levels between subjects with stiffer versus those with less stiff arteries, as reported herein, were probably underestimated. It might also be that overreporting of HPA occurred more often at older ages when health awareness may have been greater among study participants. This could explain, at least in part, the steep increases in time spent in light-to-moderate–intensity HPAs observed in this cohort, particularly after the age of 32 years. This somewhat odd trajectory of time spent in light-to-moderate HPAs can also be attributed to the change of the interview to a computerized format, which possibly captured more of these HPAs as compared with previous years. However, the increases in HPA, at least in part, may have been real, because they were accompanied by an increase in the population's mean cardiorespiratory fitness level from the age of 32 years that was measured objectively by means of maximal oxygen uptake. Importantly, however, removing HPA data at the age of 36 years from the analyses reported herein did not materially change our findings (data not shown).

Perspectives

Our findings show that vigorous but not light-to-moderate HPAs, performed and accumulated throughout the course of

life, and particularly during young adulthood, has a beneficial impact on carotid arterial stiffness later in life. Promoting increases in HPA among the healthy young as a tool to prevent arterial stiffness and related cardiovascular sequelae should, therefore, target HPAs of vigorous intensity.

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Disclosures

None.

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